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Title: Complete or incomplete coronary revascularization in patients with myocardial infarction and multivessel disease. A propensity score analysis from the "real life" BleeMACS (Bleeding complications in a Multicenter registry of patients discharged with diagnosis of Acute Coronary Syndrome) registry.

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Complete or incomplete coronary revascularization in patients with myocardial infarction and multivessel disease. A propensity score analysis from the "real life" BleeMACS (Bleeding complications in a Multicenter registry of patients discharged with diagnosis of Acute Coronary Syndrome) registry.

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ABSTRACT

Background: The benefit of complete or incomplete percutaneous coronary intervention (PCI) in patients with myocardial infarction and multivessel disease remains debated.

Methods: We conducted a multicenter study including all patients with myocardial infarction and multivessel coronary disease included in the BleeMACS (Bleeding complications in a Multicenter registry of patients discharged with diagnosis of Acute Coronary Syndrome) registry. They were divided in two groups: Complete revascularization (CR) and Incomplete Revascularization (IR). Primary endpoint was death rate at one-year follow-up. Secondary endpoints were in-hospital repeated myocardial infarction (re-AMI), in-hospital heart failure (HF), major cardiovascular events (MACE) and myocardial infarction at one year.

Results: 4520 patients were included in our analysis, the majority of them with a diagnosis of STEMI (67.7%), followed by NSTEMI (32.3%). CR was performed in 27.2% and 42.4% of them, respectively. At univariate analysis, in-hospital and one-year outcomes were similar between CR and IR in STEMI patients (all p-value >0.05). In NSTEMI patients CR was associated with a lower one-year death rate (4.5% vs 8.5%; p=0.002), re-AMI (3.7% vs 6.6%; p=0.016) and MACE (8.1% vs 13.9%; p=0.001). After propensity score, CR reduced events also in STEMI patients, including 1-year mortality (5.3% vs 13.8%; p<0.001), re-AMI (4.9% vs 17.4%; p<0.001) and MACE (8.5% vs 24.6%; p<0.001).

Conclusion: This multicentre retrospective registry showed the benefit of CR in terms of reduction one-year mortality in patients with myocardial reinfarction and multivessel coronary disease. Randomized controlled trials including functional evaluation of the lesions, should be performed to confirm our results.

CLASSIFICATION

NSTEMI, STEMI, MULTIPLE VESSEL DISEASE

CONDENSED ABSTRACT

The benefit of complete or incomplete coronary revascularization is debated in patients with myocardial infarction and multivessel disease. The present study, a sub analysis of the Bleemacs (Bleeding complications in a Multicenter registry of patients discharged with diagnosis of Acute Coronary Syndrome), retrospectively compared the two revascularization strategies in patients with myocardial infarction and multivessel coronary disease . We reported lower one-year mortality in patients undergoing complete revascularization in both STEMI and NSTEMI patients, compared to those undergoing incomplete revascularization.

ABBREVIATION

ANOVA: analysis of variance

BMS: bare metal stent

CKD: chronic kidney disease

CR: Complete revascularization

DES: drug eluting stent

FFR: fractional flow reserve

HF: heart failure

IR: Incomplete revascularization

LVEF: left ventricular ejection fraction

MACE: major cardiovascular events

NSTEMI: non ST-segment elevation myocardial infarction

PCI: percutaneous coronary intervention

Re-AMI: repeated myocardial infarction

SD: standard deviation

STEMI: ST-segment elevation myocardial infarction

INTRODUCTION

Almost half of the patients with myocardial infartcion, both those with STEMI (ST-segment elevation myocardial infarction) and those with NSTEMI (non-ST segment elevation myocardial infartcion), presents with multivessel disease [1-3], a known predictor of worse cardiovascular prognosis [4-6]

Nevertheless, the benefit of incomplete ("culprit only lesion") or complete ("culprit" and "non culprit lesions") percutaneous coronary revascularization in patients with myocardial infartcion is debated.

Although the latest European STEMI Guidelines[7] suggest the complete revascularization only for patients with cardiogenic shock or with persistent ischemia after PCI (Percutaneous coronary intervention) of the supposed culprit lesion, the randomized PRAMI[8] trial showed the superiority of a complete strategy in terms of composite cardiovascular outcomes at 23 month-follow-up. These results were confirmed by Gershlick and Colleagues in the Culprit Trial[9], and supported by a recent meta-analysis, which reported a long-term reduction in mortality of STEMI patients undergoing a multivessel staged revascularization[10].

Similarly to the STEMI setting, there is uncertainty about the strategy of percutaneous revascularization also in NSTEMI multivessel patients.
American and European Guidelines, although lacking of randomized clinical trial, consider reasonable a multivessel approach[11] or recommend to base the revascularization strategy on the clinical status and comorbidities, as well as the disease severity according to the local Heart Team protocol.[12] In the largest observational study of NSTE-ACS (non-ST segment elevation Acute Coronary Syndromes) patients with multivessel disease, which compared a "culprit only" vs a "complete revascularization"[13], rates of in hospital mortality,

bleeding, renal failure and non-fatal cardiogenic shock were similar between the groups.

The aim of our study is to compare a complete vs a “culprit only” revascularization strategy in patients with myocardial infarction distinguishing the different clinical subsets (STEMI and NSTEMI) and to provide one year clinical outcome from the “real life” BleeMACS (Bleeding complications in a Multicenter registry of patients discharged with diagnosis of Acute Coronary Syndrome) registry.

METHODS

The present study is a sub-analysis of the BleeMACS (Bleeding complications in a Multicenter registry of patients discharged with diagnosis of Acute Coronary Syndrome) project. BleeMACS is an international multicenter investigator-initiated retrospective registry, without financial support, including 15,401 ACS consecutive patients undergoing PCI and discharged alive from 15 tertiary hospitals in Europe, Asia, North and South America (Germany, Netherlands, Poland, Spain, Italy, Greece, Japan, China, Canada and Brazil) More details may be consulted in previous papers [14], in the BleeMACS webpage (http://bleemacs.wix.com/registry), or in clinicaltrials.gov (Identifier: NCT02466854).

Patients' selection

All consecutive patients with multivessel coronary disease and a diagnosis of myocardial infarction (STEMI and NSTEMI) according to ESC guidelines[12], treated with PCI during the index admission between 2003 and 2014, were eligible for inclusion. To be as possible as consistent with everyday clinical practice, no pre-specified exclusion criteria have been described.

Multivessel disease was defined as at least 70 % diameter stenosis (50% for left main) of two or more epicardial coronary arteries or their major branches by visual estimation apart from culprit lesion, with at least 2.5 mm of diameter.

Culprit lesion was defined as the coronary stenosis related to presentation with ACS according to clinical, non-invasive instrumental data (electrocardiography, echocardiography) or invasive data (Intravascular Ultrasound or Optical Coherence Tomography). These classifications were left at operator's discretion.

Patients were divided into two cohorts based upon revascularization strategy pursued at the time of presentation. Incomplete revascularization (IR group) was defined if only the

culprit lesion was treated by PCI. Complete revascularization (CR group) was defined if a final angiography result without coronary stenosis ≥ 70% in major epicardial vessels or stenosis ≥ 50% in the left main was achieved. Complete revascularization for STEMI patients was not performed during index procedure but it was staged, while for NSTEMI was performed according to operators' discretion.

Features of the patients

Baseline clinical features including age, burden of cardiovascular risk factors, presence of malignancy, history of previous bleeding, creatinine (md/dl) and haemoglobin (g/dl) were recorded.

Data about vascular access, number and type of stent (Bare Metal Stents vs. Drug Eluting Stents vs. plain Balloon Only Angioplasty) and thrombolysis were recorded.

Medications at discharge, including aspirin, choice of second anti-platelet (aspirin, clopidogrel, prasugrel and ticagrelor), use of beta-blocker, statin, Angiotensin Converting Enzyme Inhibitors, Angiotensin Receptor Blockers at discharge were recorded.

End point and follow-up

The primary end-point was all cause death at one year of follow up. Secondary endpoint included in hospital reinfarction, in-hospital heart failure, 1-year myocardial infarction and 1-year bleeding and 1-year MACE (the composite of one year death and myocardial infarction). One year bleedings were defined as any bleeding requiring hospitalization. The follow up was clinical, performed through clinical visits, phone call of formal query to primary care physicians.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD), categorical variables were expressed as number and percentages (%). Correlations between parameters and study groups were tested in cross tabulation tables by means of Pearson Chi Square test or Fisher exact test for categorical variables and by One-Way Analysis of Variance (ANOVA) for continuous variables.

Categorical variables were compared with the Fisher's exact test. Parametric distribution of continuous variables was tested graphically and with Kolmorogov Smirnov, and the appropriate analyses were used in accordance with the results. For propensity score, first logistic regression analysis was done for all baseline features that differed between CR and IR groups at univariate analysis, stratified for admission diagnosis (STEMI and NSTEMI) Matching was computed after division into quintiles and methods of nearest neighbor on the estimated propensity score.[14] Calibration was tested with Hosmer-Lermeshow, and accuracy was assessed with Area Under the Curve. Standardized differences were evaluated before and after matching to evaluate performance of the model. All statistical analyses were performed with SPSS 21 and differences were considered significant at $\alpha=0.05$.

RESULTS

Among 15401 patients in the BleeMACS registry, 4520 (29.3%) presented with a diagnosis of multivessel myocardial infarction and were included in our analysis.

The majority of patients presented with a diagnosis of STEMI (3061; 67.7%), followed by NSTEMI (1459; 32.3%) (Figure 1)

STEMI setting

Eight hundred and thirty three patients (27.2%) underwent complete coronary revascularization (CR).

Rate of women was similar in CR and IR groups (23.3% vs 20.6%; p=0.11) such as age of patients (64.1±12.0 years vs 63.9±12; p=0.60) and traditional risk factors (all p-values > 0.05). Fewer patients in CR group had history of previous myocardial infarction (9.7% vs 12.7%; p=0.02) (Table 1). No differences were found between the two groups in terms of in-hospital outcomes (all p values >0.05), 1-year death rate (5.3% vs 5.2%; p=0.89) and all secondary 1-year outcomes (all p value >0.05). (Table 2 and 3)

After propensity score with matching analysis 832 CR patients and 832 IR patients with similar baseline and procedural characteristics were selected. CR resulted superior in the prevention of 1-year death (5.3% vs 13.8%; p<0.01) such as in all the secondary 1-year outcomes (all p-value <0.05). (Table 2 and 3, Figure 2)

NSTEMI setting

Six hundred and nineteen patients (40.5%) underwent complete revascularization (CR).

Female sex was significantly higher in patients undergoing CR (26.8% vs 21.7%; p=0.02).

Traditional risk factors were comparable between the two groups (all p values >0.05)

(Table 1). One-year death rate was reduced in CR patients (4.5% vs 8.6%; p<0.01) such as occurrence of 1-year myocardial infarction (3.7% vs 6.6%; p=0.02), and of MACE (8.1% vs 13.9%; p<0.01). (Table 2 and 3)

Benefit of CR in NSTEMI patients was confirmed also after propensity score with matching analysis. (Table 2,3 and Figure 2)

DISCUSSION

To our knowledge this is one of the largest contemporaneous registries comparing complete and incomplete percutaneous revascularization in all myocardial infarction subsets in patients presenting with multivessel coronary artery disease.

The main findings in this study are:

1) Rate of death, myocardial infarction and MACE at one-year follow-up were significantly lower in STEMI and NSTEMI patients undergoing CR compared to those undergoing IR.

2) CR was safe in both STEMI and NSTEMI patients, as proved by the similar rates of in hospital and long-term bleeding.

Reperfusion strategies in patients with multi-vessel coronary disease are object of debate in the ACS setting, both in STEMI and in NSTE-ACS subgroups. The uncertainty about performing multi-vessel PCI in STEMI patients reflected an increased risk of peri-procedural complications and long-term MACE in several publications exploring cardiovascular outcomes in bare metal stent (BMS) and first generation drug eluting stnet (DES) era [16,17]. Similarly, the absence of clinical benefit was described by Hassanin and Colleagues in NSTE-ACS patients with multivessel disease[18]. Nevertheless, our result suggested a protective role in in patients with myocardial infarction.

According to STEMI patients, we reported that CR was superior to IR in terms of prevention of 1-year MACE rate. While the initial benefit of CR in STEMI patients appeared related only to a significative reduction in repeated-PCI without any influence on MACE rate[19], latest retrospective and prospective studies showed a significative reduction of 1-year major cardiovascular events[20]. In particular, Wald and colleagues[8] showed the benefit of preventive PCI in non-infarct arteries compared to a culprit only strategy, and their result

was confirmed by subsequent meta-analysis[21,22].

Moreover our analysis showed a significative reduction of myocardial infarction and death at 12 months follow-up in STEMI patients undergoing CR. These results are in accordance with those presented by a 4-randomized trials metanalysis[23], in which a multivessel revascularization strategy was associated to a significant reduction of all-cause death, cardiac death, recurrence of myocardial infarction and repeated revascularization. However the reduction of these hard end-point was not achieved by the recent DANAMI3-PRIMULTI trial[24], in which more than 600 patients were randomized after "infarct-related PCI only" to either medical therapy or fractional flow reserve guided complete revascularization: these latter benefited in terms of reduction of MACE driven by fewer repeated revascularization, but the two groups didn't no differ in all-cause mortality and non-fatal reinfarction.

NSTEMI patients undergoing complete coronary revascularization were shown to have a better 1-year cardiovascular prognosis, compared to IR patients. Both 1-year death rate, myocardial infarction and MACE were reduced by a multivessel percutaneous strategy. Differently, primary end secondary outcomes were similar between UA patients, regardless of the strategy of revascularization. While setting of multivessel disease in STEMI patients is widely investigated, randomized trials comparing different revascularization approaches in the NSTE-ACS patients are lacking; furthermore, most of the available studies have considered NSTEMI and UA as a single entity, with no risk stratification within the heterogeneous NSTE-ACS group. At this regard, a recent meta-analysis [25] investigating the complete and incomplete strategy in a miscellaneous NSTE-ACS population, showed no clinical differences in terms of long term mortality or myocardial infarction. Conversely, Onuma and Colleagues[26] showed a reduction of both

MACE and myocardial infarction or death in “NSTEMI patients only” undergoing a complete revascularization strategy, thus suggesting that a multivessel strategy could reduce hard end-points, as also showed by our analysis. The present paper, consequently, stressed the importance of a complete revascularization in a NSTEMI patients.

Our result should encourage systematic risk stratification in the NSTE-ACS group, in order to better define the PCI strategy in this heterogeneous subset.

Finally, CR was safe in all the myocardial infarction subsets as showed by the similar rates of in hospital and long term bleedings or need of transfusion between the two strategies; our results were consistent those reported in both NSTE-ACS[13] and STEMI [8,24] studies.

There are several limitations to our study mainly represented by the observational design. First the relevant proportion of STEMI patients may reflect a selection of centres focused on primary PCI. Second, while propensity score may adjust for potential recorded confounders, it may not account for differences related to causality for not recorded data, which may be avoided only by randomized controlled trial. Moreover the propensity score “selected” high risk patients as demonstrated by reduction of sample size and by similar rates of death. Third we chose a definition of non-culprit coronary stenosis on 70% with visual estimation, in order to be as adherent as possible to clinical practice, despite a frequent use in literature of definition of stenosis as critical if more than 50%[27,28]. Moreover the non-funded profile of our study lead to an adherence to real life clinical practice, although with some limitations regarding absence of central “core lab” to adjudicate events, especially in hospital death and recurrent MI. Data about interventional techniques, like fractional flow reserve (FFR) (although largely debated in ACS setting[29])were not recorded, as those about length of dual antiplatelet therapy[30]

Despite the use of appropriate statistical adjustments, differences in patient’s baseline

characteristics still remain. Moreover, since this is a subgroup analysis of the BLEEMACS registry, specific variables (e.g. diagnosis of cardiogenic shock, drugs), procedural data (e.g. type of DES, treated and untreated vessels) and outcomes (e.g. post-procedural acute kidney disease, cardiac death), were not recorded. Finally, due to the absence of adjudication by a CEC and the heterogenity of its definition, the myocardial infarction (and consequently MACE) should be considered as softer end-points

CONCLUSION

This multicentre retrospective registry showed the benefit of a complete revascularization strategy in terms of reduction of 1-year mortality in patients with myocardial infartcion and multivessel coronary artery disease, suggesting that is “better do something rather than nothing”[29].

Randomized controlled trials including functional evaluation (FFR) of the lesions, especially in the NSTE-ACS setting, should be performed to confirm our results.

IMPACT ON DAILY PRACTICE

A complete revascularization strategy could be considered in both NSTEMI e STEMi patients with multivessel coronary disease because of a significant reduction of mortality compared to an incomplete strategy.

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The authors have no conflicts of interest to declare

REFERENCES

1) D'Ascenzo F, Presutti DG, Picardi E, Moretti C, Omedè P, Sciuto F, Novara M, Yan AT, Goodman S, Mahajan N, Kosuge M, Palazzuoli A, Jong GP, Isma'eel H,Budoff MJ, Rubinshtein R, Gewirtz H, Reed MJ, Theroux P, Biondi-Zoccai G, Modena MG, Sheiban I, Gaita F.
Prevalence and non-invasive predictors of left main or three-vessel coronary disease: evidence from a collaborative international meta-analysis including 22 740 patients.
Heart. 2012 Jun;98(12):914-9

2) Sheiban I, Moretti C, D'Ascenzo F, Chieffo A, Taha S, Connor SO, Chandran S, de la Torre Hernández JM, Chen S, Varbella F, Omedè P, Iannaccone M, Meliga E, Kawamoto H, Montefusco A, Mervyn C, Garot P, Sin L, Gasparetto V, Abdirashid M, Cerrato E, Biondi Zoccai G, Gaita F, Escaned J, Hiddick Smith D, Lefèvre T, Colombo A. **Long-Term (≥10 Years) Safety of Percutaneous Treatment of Unprotected Left Main Stenosis With Drug-Eluting Stents**.
Am J Cardiol. 2016 Jul 1;118(1):32-9.

3) Fox KA, Poole-Wilson PA, Henderson RA, Clayton TC, Chamberlain DA, Shaw TR, Wheatley DJ, Pocock SJ; Randomized Intervention Trial of unstable Angina Investigators
Interventional versus conservative treatment for patients with unstable angina or non-ST-elevation myocardial infarction: the British Heart Foundation RITA 3 randomised trial. Randomized Intervention Trial of unstable Angina.
Lancet. 2002 Sep 7;360(9335):743-51.

4) Jensen LO, Terkelsen CJ, Horváth-Puhó E, Tilsted HH, Maeng M, Junker A, Lassen JF, Thuesen L, Sørensen HT, Thayssen P.
Influence of multivessel disease with or without additional revascularization on mortality in patients with ST-segment elevation myocardial infarction
Am Heart J. 2015 Jul;170(1):70-8.

5) Jaski BE, Cohen JD, Trausch J, Marsh DG, Bail GR, Overlie PA, Skowronski EW, Smith SC Jr.
Outcome of urgent percutaneous transluminal coronary angioplasty in acute myocardial infarction: comparison of single-vessel versus multivessel coronary artery disease.
Am Heart J. 1992 Dec;124(6):1427-33.

6) Sorajja P, Gersh BJ, Cox DA, McLaughlin MG, Zimetbaum P, Costantini C, Stuckey T, Tcheng JE, Mehran R, Lansky AJ, Grines CL, Stone GW.
Impact of multivessel disease on reperfusion success and clinical outcomes in patients undergoing primary percutaneous coronary intervention for acute myocardial infarction.
Eur Heart J. 2007 Jul;28(14):1709-16.

7) Task Force on the management of ST-segment elevation acute myocardial infarction of

the European Society of Cardiology (ESC), Steg PG, James SK, Atar D, Badano LP, Blömstrom-Lundqvist C, Borger MA, Di Mario C, Dickstein K, Ducrocq G, Fernandez-Aviles F, Gershlick AH, Giannuzzi P, Halvorsen S, Huber K, Juni P, Kastrati A, Knuuti J, Lenzen MJ, Mahaffey KW, Valgimigli M, van 't Hof A, Widimsky P, Zahger D.
ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation.
Eur Heart J. 2012 Oct;33(20):2569-619.

8) Wald DS, Morris JK, Wald NJ, Chase AJ, Edwards RJ, Hughes LO, Berry C, Oldroyd KG; PRAMI Investigators.
Randomized trial of preventive angioplasty in myocardial infarction.
N Engl J Med. 2013 Sep 19;369(12):1115-23.

9) Gershlick AH, Khan JN, Kelly DJ, Greenwood JP, Sasikaran T, Curzen N, Blackman DJ, Dalby M, Fairbrother KL, Banya W, Wang D, Flather M, Hetherington SL, Kelion AD, Talwar S, Gunning M, Hall R, Swanton H, McCann GP.
Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multivessel disease: the CvLPRIT trial.
J Am Coll Cardiol. 2015 Mar 17;65(10):963-72.

10) Bainey KR, Mehta SR, Lai T, Welsh RC.
Complete vs culprit-only revascularization for patients with multivessel disease undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: a systematic review and meta-analysis.
Am Heart J. 2014 Jan;167(1):1-14.

11) Amsterdam EA, Wenger NK, Brindis RG, Casey DE Jr, Ganiats TG, Holmes DR Jr, Jaffe AS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ; American College of Cardiology; American Heart Association Task Force on Practice Guidelines; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; American Association for Clinical Chemistry.
2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines.
J Am Coll Cardiol. 2014 Dec 23;64(24):e139-228.

12) Authors/Task Force members, Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, Filippatos G, Hamm C, Head SJ, Jüni P, Kappetein AP, Kastrati A, Knuuti J, Landmesser U, Laufer G, Neumann FJ, Richter DJ, Schauerte P, Sousa Uva M, Stefanini GG, Taggart DP, Torracca L, Valgimigli M, Wijns W, Witkowski A.
2014 ESC/EACTS Guidelines on myocardial revascularization: The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI).

Eur Heart J. 2014 Oct 1;35(37):2541-619.

13) Brener SJ, Milford-Beland S, Roe MT, Bhatt DL, Weintraub WS, Brindis RG; American College of Cardiology National Cardiovascular Database Registry.
Culprit-only or multivessel revascularization in patients with acute coronary syndromes: an American College of Cardiology National Cardiovascular Database Registry report.
Am Heart J. 2008 Jan;155(1):140-6.

14) D'Ascenzo F, Abu-Assi E, Raposeiras-Roubín S, Simao Henriques JP, Saucedo J, González-Juanatey JR, Wilton SB, Kikkert WJ, Nuñez-Gil I, Ariza-Sole A, Song X, Alexopoulos D, Liebetrau C, Kawaji T, Moretti C, Huczek Z, Nie SP, Fujii T, Correia LC, Kawashiri MA, García-Acuña JM, Southern D, Alfonso E, Terol B, Garay A, Zhang D, Chen Y, Xanthopoulou I, Osman N, Möllmann H, Shiomi H, Giordana F, Scarano S, Gaita F, Kowara M, Filipiak KJ, Wang X, Yan Y, Fan JY, Ikari Y, Nakahayshi T, Sakata K, Yamagishi M, Kalpak O, Kedev S.
BleeMACS: rationale and design of the study.
J Cardiovasc Med (Hagerstown). 2016 Jan 27. [Epub ahead of print]

15) D'Ascenzo F, Cavallero E, Biondi-Zoccai G, Moretti C, Omedè P, Bollati M, Castagno D, Modena MG, Gaita F, Sheiban I.
Use and misuse of multivariable approaches in interventional cardiology studies on drug-eluting stents: a systematic review.
J Interv Cardiol. 2012 Dec;25(6):611-21.

16) Abe D, Sato A, Hoshi T, Takeyasu N, Misaki M, Hayashi M, Aonuma K.
Initial culprit-only versus initial multivessel percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction: results from the Ibaraki Cardiovascular Assessment Study registry.
Heart Vessels. 2014 Mar;29(2):171-7

17) Meliga E, Fiorina C, Valgimigli M, Belli R, Gagnor A, Sheiban I, Resmini C, Tizzani E, Aranzulla T, Scrocca I, DE Benedictis M, Conte MR.
Early angio-guided complete revascularization versus culprit vessel PCI followed by ischemia-guided staged PCI in STEMI patients with multivessel disease.
J Interv Cardiol. 2011 Dec;24(6):535-41.

18) Hassanin A, Brener SJ, Lansky AJ, Xu K, Stone GW.
Prognostic impact of multivessel versus culprit vessel only percutaneous intervention for patients with multivessel coronary artery disease presenting with acute coronary syndrome.
EuroIntervention. 2015 Jul;11(3):293-300.

19) Moretti C, D'Ascenzo F, Quadri G, Omedè P, Montefusco A, Taha S, Cerrato E, Colaci C, Chen SL, Biondi-Zoccai G, Gaita F
Management of multivessel coronary disease in STEMI patients: a systematic review and meta-analysis.

Int J Cardiol. 2015 Jan 20;179:552-7.

20) Rodrigues G, de Araújo Gonçalves P, Madeira S, Rodrigues R, Borges Santos M, Brito J, Raposo L, Mesquita Gabriel H, Campante Teles R, Almeida M, Mendes M.
Impact of complete revascularization in patients with ST-elevation myocardial infarction: analysis of a 10-year all-comers prospective registry.
Coron Artery Dis. 2015 Dec 18.

21) Dahal K, Rijal J, Panta R, Lee J, Azrin M, Lootens R.
Multi-vessel versus culprit-vessel and staged percutaneous coronary intervention in STEMI patients with multivessel disease: a meta-analysis of randomized controlled trials.
Cardiovasc Revasc Med. 2014 Nov-Dec;15(8):408-13.

22) Bangalore S, Toklu B, Wetterslev J.
Complete versus culprit-only revascularization for ST-segment-elevation myocardial infarction and multivessel disease: a meta-analysis and trial sequential analysis of randomized trials.
Circ Cardiovasc Interv. 2015 Apr;8(4).

23) El-Hayek GE, Gershlick AH, Hong MK, Casso Dominguez A, Banning A, Afshar AE, Herzog E, Tamis-Holland JE.
Meta-Analysis of Randomized Controlled Trials Comparing Multivessel Versus Culprit-Only Revascularization for Patients With ST-Segment Elevation Myocardial Infarction and Multivessel Disease Undergoing Primary Percutaneous Coronary Intervention.
Am J Cardiol. 2015 Jun 1;115(11):1481-6.

24) Engstrøm T, Kelbæk H, Helqvist S, Høfsten DE, Kløvgaard L, Holmvang L, Jørgensen E, Pedersen F, Saunamäki K, Clemmensen P, De Backer O, Ravkilde J, Tilsted HH, Villadsen AB, Aarøe J, Jensen SE, Raungaard B, Køber L; DANAMI-3—PRIMULTI Investigators.
Complete revascularisation versus treatment of the culprit lesion only in patients with ST-segment elevation myocardial infarction and multivessel disease (DANAMI-3—PRIMULTI): an open-label, randomised controlled trial.
Lancet. 2015 Aug 15;386(9994):665-71.

25) Mariani J,2, Macchia A, De Abreu M, Gonzalez Villa Monte G, Tajer C.
Multivessel versus Single Vessel Angioplasty in Non-ST Elevation Acute Coronary Syndromes: A Systematic Review and Metaanalysis.
PLoS One. 2016 Feb 17;11(2):on press

26) Onuma Y, Muramatsu T, Girasis C, Kukreja N, Garcia-Garcia HM, Daemen J, Gonzalo N, Piazza N, Einthoven J, van Domburg R, Serruys PW
Interventional cardiologists of the Thoraxcenter (2000-5). Single-vessel or multivessel PCI in patients with multivessel disease presenting with non-ST-elevation acute coronary syndromes.

Eurointervention 2013 Dec;9(8):916-22.

27) Cowley MJ, Vandermael M, Topol EJ, Whitlow PL, Dean LS, Bulle TM, Ellis SG.
Is traditionally defined complete revascularization needed for patients with multivessel disease treated by elective coronary angioplasty? Multivessel Angioplasty Prognosis Study (MAPS) Group.
J Am Coll Cardiol. 1993 Nov 1;22(5):1289-97.

28) Généreux P, Palmerini T, Caixeta A, Rosner G, Green P, Dressler O, Xu K, Parise H, **Mehran R, Serruys PW, Stone GW. Quantification and impact of untreated coronary artery disease after percutaneous coronary intervention: the residual SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) score**.
J Am Coll Cardiol. 2012 Jun 12;59(24):2165-74.

29) Layland J, Oldroyd KG, Curzen N, Sood A, Balachandran K, Das R, Junejo S, Ahmed N, Lee MM, Shaukat A, O'Donnell A, Nam J, Briggs A, Henderson R, McConnachie A, Berry C; FAMOUS–NSTEMI investigators.
Fractional flow reserve vs. angiography in guiding management to optimize outcomes in non-ST-segment elevation myocardial infarction: the British Heart Foundation FAMOUS-NSTEMI randomized trial.
Eur Heart J. 2015 Jan 7;36(2):100-11.

30) D'Ascenzo F, Moretti C, Bianco M, Bernardi A, Taha S, Cerrato E, Omedè P, Montefusco A, Frangieh AH, Lee CW, Campo G, Chieffo A, Quadri G, Pavani M, Zoccai GB, Gaita F, Park SJ, Colombo A, Templin C, Lüscher TF, Stone GW.
Meta-Analysis of the Duration of Dual Antiplatelet Therapy in Patients Treated With Second-Generation Drug-Eluting Stents.
Am J Cardiol. 2016 Jun 1;117(11):1714-23.

FIGURE LEGENDS

Figure 1. STEMI and NSTEMI patients distribution before and after propensity score matching analysis

Figure 2. STEMI and NSTEMI patients outcomes after propensity score matching analysis.

TABLE LEGENDS

Table 1. Baseline features of STEMI and NSTEMI patients before and after propensity score matching analysis.

Table 2. Outcomes in STEMI and NSTEMI patients before and after propensity score matching analysis.

Table 3. Rates of in-hospital and 1-year myocardial infarction and 1-year MACE in STEMI and NSTEMI patients before and after propensity score matching analysis.

Table 1. Baseline features of STEMI and NSTEMI patients before and after propensity score matching analysis.

	BEFORE PROPENSITY			AFTER PROPENSITY		
	Multivessel PCI	**Cultprit only PCI**	**P value**	**Multivessel PCI**	**Culprit only PCI**	**P value**
STEMI	**n= 833**	**n=2228**		**n=813**	**n=813**	
Female	194 (23.3%)	459 (20.6%)	0.106	189 (23.2%)	185 (22.8%)	0.81
Age (years)	64.1±12.0	63.9±12.3	0.599	64.1±12.0	65.9±11.6	0.67
Diabetes	193 (23.2%)	544 (24.4%)	0.473	210 (26.4%)	228 (28.0%)	0.06
Hypertension	477 (57.3%)	1236 (55.5%)	0.375	464 (57.1%)	450 (55.4%)	0.48
Dislipidemia	385 (46.2%)	1007 (45.2%)	0.614	378 (46.5%)	358 (44.7%)	0.07
LVEF (%)	50.1±11.8	50.6±11.7	0.400	50.1±11.9	50.0±11.5	0.48
Prior AMI	81 (9.7%)	283 (12.7%)	0.02	79 (9.7%)	116 (14.3%)	0.09
CKD	10 (4.1%)	17 (5.3%)	0.495	10 (4.1%)	17 (5.3%)	0.49
Killip 2	149 (18.3%)	333 (15.4%)	0.050	149 (18.3%)	187 (23.0%)	0.06
Femoral. access	487 (58.5%)	1597 (71.7%)	<0.001	473 (58.2%)	452 (55.6%)	0.29
DES	334 (40.1%)	1003 (45.0%)	0.015	327 (40.2%)	289 (.5%)	0.05
No stent PCI	17 (2.1%)	114 (5.0%)	<0.001	17 (2.1%)	24 (3.2%)	0.08
NSTEMI	**n= 619**	**n= 840**		**n=609**	**n=609**	
Female	166 (26.8%)	182 (21.7%)	0.02	166 (26.8%)	134 (22.0%)	0.05
Age (years)	68.7±12.2	68.1±11.5	0.38	68.7±12.2	67.8±11.5	0.22
Diabetes	221 (35.7%)	333 (39.6%)	0.12	221 (35.7%)	232 (38.1%)	0.38
Hypertension	443 (71.6%)	587 (69.9%)	0.48	443 (71.6%)	394 (64.7%)	0.09
Dislipidemia	338 (54.6%)	477 (56.8%)	0.41	338 (54.6%)	336 (55.2%)	0.84
LVEF (%)	51 (8.2%)	122 (14.5%)	<0.01	52.6±12.2	54.0%±11.8	0.05
Prior AMI	120 (19.4%)	199 (23.7%)	0.05	120 (19.4%)	109 (17.9%)	0.50
CKD	17 (6.4%)	40 (8.2%)	0.38	17 (6.4%)	35 (7.7%)	0.52
Killip 2	149 (18.3%)	187 (23.0%)	0.06	92 (15.7%)	100 (17.1%)	0.51
Femoral access	288 (46.5%)	377 (44.9%)	0.53	288 (46.5%)	270 (44.5%)	0.09
DES	280 (45.2%)	368 (43.8%)	0.59	280 (45.2%)	244 (40.1%)	0.07
No stent PCI	3 (0.5%)	49 (5.8%)	<0.01	10 (2.5%)	15 (3.1%)	0.67

Table 2. Outcomes in all ACS subgroups before and after propensity score matching analysis.

	BEFORE PROPENSITY			AFTER PROPENSITY		
	Multivessel PCI	**Cultprit only PCI**	**P value**	**Multivessel PCI**	**Culprit only PCI**	**P value**
STEMI	**n= 833**	**n=2228**		**n=813**	**n=813**	
in hospital HF	52 (7.3%)	134 (8.3%)	0.42	51 (7.4%)	57 (8.9%)	0.32
In hospital bleeding	66 (7.9%)	163 (7.3%)	0.57	63 (7.7%)	86 (10.6%)	0.05
In hospital transfusion	35 (4.8%)	91 (5.4%)	0.57	34 (4.8%)	48 (6.0%)	0.31
1-year death	44 (5.3%)	115 (5.2%)	0.89	43 (5.3%)	112 (13.8%)	<0.01
1-year bleeding	21 (2.5%)	78 (3.5%)	0.17	21 (2.6%)	37 (3.6%)	<0.01
NSTEMI	**n= 619**	**n= 840**		**n=609**	**n=609**	
in hospital HF	34 (5.5%)	56 (6.7%)	0.357	34 (5.5%)	36 (5.9%)	0.75
In hospital bleeding	39 (6.3%)	71 (8.5%)	0.124	39 (6.3%)	42 (6.9%)	0.67
In hospital transfusion	28 (4.6%)	49 (5.9%)	0.303	28 (4.6%)	34 (5.6%)	0.44
1-year death	28 (4.5%)	72 (8.6%)	<0.01	28 (4.5%)	63 (10.3%)	<0.01
1-year bleeding	22 (3.6%)	38 (4.5%)	0.357	22 (3.6%)	26 (4.3%)	0.52

Table 3.
Rates of in-hospital and 1-year myocardial infarction and 1-year MACE in STEMI and NSTEMI patients before and after propensity score matching analysis.

	BEFORE PROPENSITY			AFTER PROPENSITY		
	Multivessel PCI	**Cultprit only PCI**	**P value**	**Multivessel PCI**	**Culprit only PCI**	**P value**
STEMI	**n= 833**	**n=2228**		**n=813**	**n=813**	
in hospital reAMI	13 (1.6%)	38 (1.7%)	0.78	13 (1.6%)	22 (2.7%)	0.12
1-year reAMI	40 (4.8%)	140 (6.3%)	0.11	40 (4.9%)	139 (17.4%)	<0.01
1-year MACE	70 (8.4%)	204 (9.2%)	0.52	69 (8.5%)	200 (24.6%)	<0.01
NSTEMI	**n= 619**	**n= 840**		**n=609**	**n=609**	
in hospital reAMI	10 (1.6%)	23 (2.7%)	0.153	10 (1.6%)	17 (2.8%)	0.16
1-year reAMI	23 (3.7%)	55 (6.6%)	0.02	23 (3.7%)	55 (9.1%)	<0.01
1-year MACE	50 (8.1%)	117 (13.9%)	<0.01	50 (8.1%)	108 (17.7%)	<0.01

Figure 1.

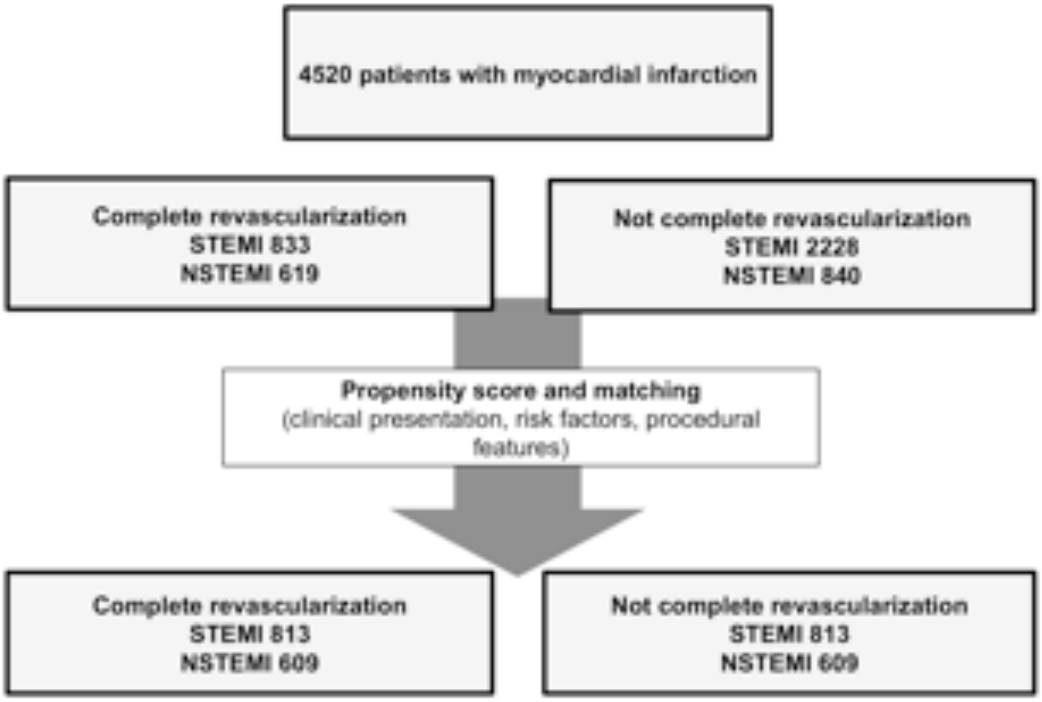

Figure 2.